

and possibly all reactions is lower. In summary, the drug is less toxic but also less effective than diphenylhydantoin.

Usual Dosage.—*Oral: Adults:* Initially, 1 gm daily in divided doses; for maintenance, 2 to 3 gm daily in four to six divided doses. *Children:* 0.5 to 1 gm daily in divided doses.

Preparations.—Peganone (Abbott): Tablets 250 and 500 mg.

Mephénytoin [MESANTOIN]

Effective in major motor and psychomotor epilepsy, but more dangerous than diphenylhydantoin and thus should be reserved for cases refractory to the drugs of choice. Has a sedative effect usually absent with diphenylhydantoin; otherwise lacks or has lower incidence of some of the more minor adverse effects of diphenylhydantoin (eg, ataxia, gingival hyperplasia, hirsutism, gastric distress). However, life-threatening and other serious reactions are considerably more common: severe skin eruptions, blood dyscrasia (eg, aplastic anemia, leukopenia, agranulocytosis, thrombocytopenia, megaloblastic anemia), liver damage, lupus erythematosus, and pseudolymphoma.

Usual Dosage.—*Oral: Adults:* Initially, 50 to 100 mg daily, with weekly increases of the same amount until maintenance dose, usually 200 to 600 mg, is established. Further increases to 800 mg or more occasionally required. *Children:* Initially as for adults; maintenance dose usually 100 to 400 mg, depending on age of patient and severity of seizures.

Preparations.—Mesantoin (Sandoz): Tablets 100 mg.

Succinimides

Ethosuximide [ZARONTIN]

Drug of choice for petit mal. Also effective for minor motor seizures in some patients, but generally ineffective for psychomotor or grand mal epilepsy, or in patients with considerable organic brain damage.

Major untoward effects appear to be less frequent than with trimethadione or paramethadione; the most frequent are gastrointestinal disturbances. Drowsiness, ataxia, headache, dizziness, euphoria, hiccup, skin eruptions, and psychologic or psychiatric aberrations have been reported. Aplastic anemia, thrombocytopenia, leukopenia, pancytopenia, and eosinophilia have been reported rarely. See the monograph in the New Drugs section for further details.

Usual Dosage.—*Oral: Adults and Children over 6:* 500 mg daily initially; increase daily dose by 250 mg every one to two weeks until seizures are controlled or untoward effects develop. Dosages exceeding 1 gm per day are seldom more effective than smaller dosages. *Children under 6:* Initial daily dosage is 250 mg.

Preparations.—Zarontin (Parke, Davis): Capsules 250 mg.

Methsuximide [CELONTIN]

May be helpful in petit mal and minor motor seizures, especially when used with other anticonvulsants. Also may be used as the second or third drug to reduce the incidence of psychomotor attacks. Grand mal, if present, must be controlled with other medication. Untoward effects occur frequently and may be of minor or major consequence. These include gastrointestinal disturbances and reactions affecting the central nervous system (drowsiness, headache, dizziness, diplopia, and ataxia). Hypersensitivity reactions, such as skin eruptions, fever, hiccup, and periorbital hyperemia, occur only rarely. Many minor untoward effects may disappear spontaneously or be controlled by reducing dosage, but a rash may herald a more serious reaction. Severe mental depression may occur, and patients who have psychomotor seizures particularly should be watched closely for behavioral changes, for these may progress to an acute psychosis unless the drug is discontinued. Renal and hepatic damage may occur. Hematologic reactions, including aplastic anemia, although rare, have also been reported.

Usual Dosage.—*Oral: Adults and Children:* Initially, 300 mg daily; this may be increased at weekly intervals until a daily dose of 1.2 gm, given in divided amounts, is attained. The optimal dose is the minimal amount that will control seizures without causing serious untoward effects.

Preparations.—Celontin (Parke, Davis): Capsules 150 and 300 mg.

Phensuximide [MILONTIN]

Used in control of petit mal seizures. Less effective and less potent than ethosuximide and trimethadione. However, it is the safest of the succinimides. Its relative lack of serious toxicity justifies its inclusion among drugs that may be considered for initial trial in petit mal (see general statement), although substitution of a more effective agent usually will be necessary. Adverse effects may include nausea, weakness, drowsiness, and skin eruptions. The confirmed reaction of greatest concern reported to date is nephropathy, particularly in children, which apparently is reversible on withdrawal of the drug. Agranulocytosis, if indeed it is caused by this drug, has been very rare.

Usual Dosage.—*Oral: Adults and Children:* 500 mg to 1 gm two or three times daily.

Preparations.—Milontin (Parke, Davis): Capsules 250 and 500 mg; suspension 250 mg/4 ml.

Oxazolinediones

Trimethadione [TRIDIONE]

Principally effective in control of petit mal seizures. Although among the more effective agents for this purpose, should be reserved for refractory cases because of toxicity. Serious reactions, some of them fatal, include skin eruptions that may progress to exfoliative dermatitis or erythema multiforme, nephropathy, hepatitis, and marrow depression with aplastic anemia, neutropenia, or